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LEADING ARTICLE

Health Surveillance in Europe: Lessons from EUROCAT and Chernobyl

H DOLK* AND M F LECHAT†

Chernobyl (26 April 1986) was a major public health disaster, but the accident has further significance in the context of surveillance systems in Europe. Chernobyl is a natural experiment of the effects of radiation, particularly low-dose radiation. It could be exploited in order to improve our assessment of risk, mainly based until now on high exposures from Hiroshima and medical procedures. Chernobyl is a test for health information systems—can they respond to the questions asked of them about the relation between a radiation exposure incident and health? Chernobyl is also a warning that such accidents and worse are possible and that the public health world must be prepared. In all these respects, what is needed is a co-ordinated European response.

Europe is as yet at a very early stage in working out an international surveillance mechanism. EUROCAT is a prototype for European surveillance. It was set up in 1979 as a Concerted Action of the EC for the epidemiological surveillance of congenital anomalies. It was initially an experiment in European surveillance, to assess the feasibility of pooling data across national boundaries, both in terms of standardization of definitions, diagnosis and terminology, and in terms of confidentiality.

EUROCAT is based on a network of regional registries, co-ordinated by a central registry in Brussels. In 1991, 25 registries in 14 countries of Europe were participating in the network, covering all together approximately 350000 births per year or a roughly 10% sample of the countries in which they are situated (Table 1). Regional registries were preferred over national registries so as to collect higher quality data for well-defined small to medium-sized populations, which could then be pooled across Europe, sharing the cost of the enterprise. However, it can be as useful to compare and contrast findings between registries, as it is to pool data across Europe.

The EUROCAT registries follow a clear set of underlying principles although each registry designed a system that would embody these principles under local conditions.[1] Registries were to be population-based, use multiple sources of information for case ascertainment and for the validation and elaboration of diagnoses, collect a common data set, use standard terminology and definitions, and extend ascertainment beyond the first week of life and if possible up to 1 year or into childhood. This intensive data collection effort also enabled many registries to incorporate data on terminations of pregnancy following prenatal diagnosis of congenital anomalies, which during the 1980s were becoming increasingly frequent and therefore essential to any effective surveillance system (Table 2).[2]

HOW DID EUROCAT RESPOND TO CHERNOBYL?

A report prepared for the Commisson of the European Communities[3] estimated that average adult effective dose from Chernobyl in the first year in the European Community ranged from 0.2 microSv in Portugal and Spain to 150–300 microSv in Germany, Italy and Greece. The dose to the critical group, that is the fraction of the population with the highest level of exposure, was estimated to be about 10 times higher. The main routes of exposure were external radiation from deposited material and internal irradiation from ingestion of contaminated foodstuffs and inhalation of the material from the cloud.

These estimated exposures are of the same order as *background radiation and weapons testing in the* 1960s,[4] and below the International Committee on Radiological Protection (ICRP) guidelines for the ex-

* Environmental Epidemiology Unit, London School of Hygiene and Tropical Medicine, Keppel St, London WC1E 7HT, UK.
† Department of Epidemiology, Catholic University of Louvain, Brussels, Belgium.

TABLE 1 *EUROCAT population coverage 1991*

Country	Approximate total annual births	Registry	Estimated registry coverage No. births	Coverage %
Belgium	118000	West Flanders	9400	8.0
		Hainaut	13 500	11.4
		Antwerp[a]	5000	4.2
		Total	27900	23.6
Denmark	59000	Odense	4900	8.3
France	775000	Paris	37000	4.8
		Strasbourg	13500	1.7
		Marseilles	23800	3.1
		Total	74300	9.6
Italy	556000	Firenze	8900	1.6
		Umbria	6600	1.2
		Emilia Romagna	22800	4.1
		Veneto	52200	9.4
		Total	90500	16.3
Ireland	62000	Dublin	18700	30.2
		Galway[a]	2800	4.5
		Total	21500	34.7
Luxemburg	4900	Luxemburg	4410	90.0
Malta	5500	Malta	5500	100.0
Netherlands	188000	Groningen	19700	10.5
		Rotterdam[a]	7000	3.7
		Total	26700	14.2
Portugal	125000	Beja	5600	4.5
UK	780000	Glasgow	12 900	1.7
		Belfast	26300	3.4
		Wales[a]	10500	1.3
		Total	49700	6.4
Spain	436000	Bilbao[a]	11600	2.7
Switzerland	81000	Switzerland	53000	65.4
Croatia	67000	Zagreb	8000	11.9
Total	3257400		383610	11.8

[a] Registries expanding since 1991.

posure of pregnant women in the workplace of 5000 microSv per year. However, these comparisons are quite difficult,[5] because it is preferable to take into account the type of radionuclide and route of exposure, and especially for teratogenic effects, the range of exposures in the population rather than the average. In addition, a short burst of exposure may be different in its mutagenic or teratogenic potential than similar exposure levels spread throughout the year.

The EUROCAT response to Chernobyl was precipitated by two reports of clusters. The first concerned a cluster of Down's syndrome in West Berlin.[6] In January 1987, 9 months after Chernobyl, 10 cases of trisomy 21 were diagnosed among livebirths, rather than the average of two cases per month observed since 1980, after which the rate returned to normal.

The second report concerned a cluster of neural tube defects (NTD) in Turkey.[7] In one maternity hospital in Bursa, Turkey, 12 cases of NTD were found in the first 6 months of 1987, when only 3–4 would have been expected on the basis of records held since 1983. Another cluster was found in a maternity unit in Izmir,[8] but two other maternity units in Turkey later reported that they could find no increase.[9,10]

TABLE 2 *Percentage of total cases of five congenital anomalies which were prenatally diagnosed with subsequent termination of pregnancy, 10 EUROCAT registries, 1986–1988*

Registry, period and No. births	Anencephaly	Spina bifida	Bilateral renal agenesis	Omphalocoele	Down's syndrome	Down's syndrome maternal age ⩾35
	%	%	%	%	%	%
Hainaut, Belgium 1986–1988; 25703	94.1	0.0	(66.7)[a]	(50.0)[a]	13.8	(50.0)[a]
Odense, Denmark 1986–1988; 14736	50.0	18.2	(0.0)[a]	(0.0)[a]	15.2	55.6
Paris, France 1986–1988; 109136	80.0	56.8	52.4	43.2	33.9	50.0
Strasbourg, France 1986–1988; 39598	76.9	44.4	40.0	46.2	26.7	54.2
Marseille, France 1986–1987; 46887	81.8	52.4	58.3	41.7	20.0	31.6
Florence, Italy 1986–1988; 25718	91.7	70.0	16.7	(0.0)[a]	20.0	33.3
Groningen, NL 1986–1988; 35378	62.5	8.7	13.3	33.3	21.4	50.0
Glasgow, UK 1986–1988; 38977	88.4	52.9	31.2	45.8	19.6	58.3
Liverpool, UK 1986–1987; 41262	86.4	54.5	11.1	40.0	0.0	0.0
Belfast, UK 1986–1987; 56313	51.5	5.2	7.1	16.7	4.9	11.4

[a] Percentages based on ⩽5 total cases.
Based on EUROCAT Report 4[2]

If we imagine that medical personnel across Europe were each searching in their patch for an effect of Chernobyl in the subsequent 9 months, it is inevitable, just by the laws of probability, that isolated clusters would be found, and these clusters are of course more likely to be published than negative findings. In this context it is difficult to judge the significance of the clusters in Berlin and Turkey. The importance of a larger surveillance system was to provide a unified and systematic approach to see whether a general or dose-related post-Chernobyl phenomenon could be found.

In 1987 preliminary analyses of the EUROCAT data were performed to provide a prompt reply to these reports.[11-13] The first analysis, in May 1987, concerned Down's syndrome and was therefore looking for preconceptional mutagenic effects. The comparison was between conceptions before Chernobyl and those occurring during or after Chernobyl. It is worth noting that the literature on the relationship between radiation exposure and Down's syndrome is not at all clear, and in particular does not clarify the significance of the timing of exposure in relation to conception. Some epidemiological studies have concerned radiation exposure close to the time of conception, and others have concentrated more on cumulative exposure over many years. To complicate matters even further, the pattern of exposure after Chernobyl is itself quite complex, with relatively high exposure in the first few weeks from external radiation and then a build up of exposure from internal radiation which came to its peak only in early to mid 1987.[14-18]

The EUROCAT investigation identified 621 live-births, stillbirths and induced abortions with Down's syndrome, registered from January 1986 to March 1987, in a total population of 482200 births. The monthly rates of Down's syndrome conceptions were calculated by date of conception from May 1985 to June 1986. There was no increase in rate after Chernobyl, but a slight decrease in rate related to delay in case finding in the more recent post-Chernobyl period. Comparing cases conceived before 1 May 1986 to those conceived after, there was no significant variation in the ratio of free trisomy to translocation trisomy 21.

The anomalies selected for the second analysis in October 1987 included NTD as reported in Turkey, but also included other central nervous system and eye defects, since it is for these groups of defects that there is most evidence for radiation effects. Microcephaly in particular was found at a high frequency in the population in utero at the time of the Hiroshima bomb, for those close to the hypocentre.[19]

The analysis of central nervous system and eye anomalies had to take a slightly different approach from that of Down's syndrome since it was looking for postconceptional teratogenic effects rather than preconceptional mutagenic effects. The time of conception was also taken as the reference point, but the relevant exposure time is exposure during the sensitive period of development. These sensitive periods were set at 3–5 weeks postconception for NTD and arrhinencephaly and 3–16 weeks postconception for microcephaly, hydrocephaly, cataract and anophthalmos or microphthalmos. Exposure was then defined as being in a sensitive period during the first 2 months after Chernobyl, or during the first 5 months after Chernobyl. This second period was to take into account more exposure from internal radiation, although it did not yet include the period of peak internal exposure a year after the accident.

The observed numbers of cases in the exposed cohorts were compared to the expected numbers calculated for each registry from the 1980–1985 registration period. Pooling all the centres together gave no significant increase,[13] nor was there any dose-related increase when centres were ranked in order of relative exposure.[20] Among the individual registries, there was a significant increase of NTD in Odense, Denmark, for the cohort exposed within 2 months of Chernobyl with four cases observed and 0.9 cases expected.[13] In interpreting this finding it should be remembered that Odense was not one of the more exposed areas, the increase was not found for microcephaly (which is thought to be the most sensitive indicator of radiation exposure), and it would not be unexpected to find one increased rate among multiple comparisons. The relevance of this cluster remains an open question.

HOW WELL COULD EUROCAT RESPOND TO CHERNOBYL?

Chernobyl was a test for EUROCAT as a European health information system. To evaluate its response we can look at the range of outcomes measured, the quality of the information on each outcome, the coverage of exposed populations, the delay between the accident and the availability of health information, the sensitivity of surveillance and the ability to ensure confidentiality of medical data.

Our main hypotheses concerned mutagenic effects of radiation and teratogenic effects on the developing central nervous system and eye. The measurable endpoints were Down's syndrome, microcephaly, NTD, hydrocephaly, and eye malformations. It should be noted that EUROCAT is not an information system about reproductive endpoints in general, but only about congenital anomalies in their most classic sense. Thus we had no information on spontaneous abortions (malformed or normal), birthweight, or perinatal or infant mortality, nor on mental retardation which manifests later in childhood, even when of congenital origin. Mental retardation, even more than microcephaly, is the best documented teratogenic effect of radiation in Hiroshima and Nagasaki.[21]

The completeness of case ascertainment in the EUROCAT system varies between registries and between malformations. An unpublished audit of Down's syndrome rates in the various registries 1980–1986 compared to an external Swedish standard[22] showed for the 46% sample of the coverage for which accurate maternal age denominator information was available that average EUROCAT rates were lower in the <30 year age group ($O/E = 0.84$) but equivalent or slightly higher in the >30 age group. The discrepancy among younger mothers may of course be a true reflection of lower risk, and was not restricted to any identifiable subset of registries.

A particular issue in case ascertainment, particularly for Down's syndrome and NTD, is the registration of induced abortions following prenatal diagnosis. In the audit of Down's syndrome mentioned above, underregistration of induced abortions was a problem for only 8% of the population included in the audit. In the post-Chernobyl surveillance, however, nonregistration or underregistration of induced abortions was a major limitation. The three regions with highest exposure among the EUROCAT regions, i.e. northeast Italy, Emilia Romagna and Zagreb, happened not to register induced abortions. This would tend to lower the sensitivity of the analysis but would only produce a bias if the rate of prenatal diagnosis changed after Chernobyl, whether because of the accident or because of new developments in the screening services. This emphasizes the importance of including induced abortions in congenital anomaly surveillance systems.

Unfortunately, there are no 'quick fixes' for the assessment of completeness of ascertainment, since the 'true' local prevalence is rarely known (as in the Down's syndrome example given), since cases are rarely 'randomly' lost to the system (allowing capture-

recapture methods of assessment), and since problems of case definition may obscure ascertainment. A detailed knowledge of how a baby with each type of malformation is catered for by the medical system, the sources of information used by the registry and the level of communication between registry and clinicians always needs to accompany any statistical approach. Inevitably this knowledge is greater in the local registries than in the central registry. Comparisons of prevalence rates and case characteristics between registries, however, have been found to be an invaluable tool in the assessment of ascertainment.[2,23] EUROCAT's two-tier structure with independent local registries feeding into a central registry seems well-adapted to the maintenance and improvement of ascertainment levels.

Perhaps the greatest problem in the post-Chernobyl surveillance was the inadequacy of surveillance of microcephaly. Lack of standardization of the definition of microcephaly, not only from region to region but from clinician to clinician, was shown by a survey made in EUROCAT registries in 1984.[24] In addition, microcephaly is rarely a diagnosis made from one measurement in the neonatal period. There can be catch-up growth as well as retardation of head growth in the early postnatal period and ascertainment should be extended to the end of the first year of life. This obviously constrains the speed with which the data can be collected after the exposure of concern, and also limits the comparability of different populations with different ascertainment methods and operational definitions.

The problem of microcephaly leads us to question the feasibility of imposing true standardization on heterogeneous medical diagnostic definitions across Europe. Having identified that there is a problem, what do we then do? It is a problem of health information systems that the flow of information and change in diagnostic definitions tends to go one way. The information system abstracts information from the medical world, but does not feed back into the medical world to change its practices. In the case of microcephaly, there is even a degree of incompatibility between the definition needs of epidemiological surveillance and the definition needs of clinicians. The role of EUROCAT to date has been mainly to identify the problems, and to try to promote consensus meetings between European clinicians.

In 1987, EUROCAT was covering a sample of approximately 10% of the births in the European countries represented, but the regions with relatively high exposure for Western Europe were under-represented. It is virtually impossible to devise a system which will be representative for all possible exposures. Nevertheless, we believe that the disadvantages of not being comprehensive are more than outweighed by the advantages in terms of data quality, of restricting data collection to selected regions. For selected anomalies, this is not the only possible model. For Down's syndrome, for example, which is a well-defined anomaly and where the vast majority of cases have cytogenetic confirmation, it is feasible to collect data on a national level, based on cytogenetic laboratory reports. Such a system is proving quite successful in England and Wales.[25]

In our experience, an international system does not make for rapid routine monitoring. The system tends to be held back by the slow registries, and it is difficult to be kept informed about delays being experienced at local level so as to be able to adjust for them. Both the Down's syndrome and the central nervous system studies were done in 1987 and required that data be sent outside the usual transmission channels in order to provide a more rapid answer. Especially for Down's syndrome, which was analysed earlier, there was a trend towards underascertainment in the most recent period analysed, which corresponded to the exposure period. At the end of 1992 we expect to perform a final analysis, including all registries and well validated information, and an exposure period which will include the peak internal radiation experienced in mid-1987.

The implications of this delay for the general monitoring functions of EUROCAT is that an 'early warning system' is not feasible at central level, but should be carried out locally. The function of the central registry in this 'early warning' system is to provide fast channels of communication for the results of local monitoring, a communication which can be effective because of the constant validation and comparison of data between regions going on at central level. In special circumstances like Chernobyl, this network can be activated to produce a co-ordinated, if preliminary, response very much more quickly than would be possible without it.

The sensitivity of surveillance, or its ability to detect a true increase in rates, is partially dependent on some of the aspects already discussed, particularly the quality of information on outcomes. We can also assess the sensitivity in terms of the statistical power of the pooled analysis to detect a small increase. Given a Type I error of 5% and a power of 80%, the minimum detectable factor of increase in the risk for the 5-month cohort of approximately 100000 pregnancies, in the central nervous system analysis, would be 2.4 for defects with a frequency of the order of 0.5 per 10000 (arrhinencephaly) and 1.2 for defects with frequency

of the order of 1 per 1000 (NTD). (For a generalized exposure like Chernobyl radiation, the latter relative risk of 1.2 implies an excess of about 700 cases across the European countries in which there are EUROCAT registries). These minimum detectable risk increases for an individual registry with a 10000 birth cohort size over 5 months would be 7.6 and 1.9 for the less and more frequent anomalies respectively, demonstrating the increased statistical power of pooling.

Confidentiality of medical data in international surveillance is a difficult issue especially in view of new European legislation which is alarming epidemiologists.[26] At present EUROCAT local registries work with their local confidentiality requirements, and data transmission to Brussels is of anonymized records only.

CONCLUSIONS

EUROCAT surveillance post-Chernobyl has not suggested a general increase in the frequency of Down's syndrome or central nervous system anomalies in Western Europe. The experience has demonstrated that a European surveillance system is possible, is an effective means of addressing environmental concerns of an international nature and gives 'added value' to local surveillance systems. However, it has also highlighted some of the deficiences in health information systems related to congenital anomalies which need to be addressed both from within the EUROCAT system and outside it. Surveillance should not be seen as a secondary product of clinical activity, but rather requires dialogue between clinicians and epidemiologists.

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